UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/668,665	09/23/2003	Jean-Claude Yvin	P08425US00/BAS	1061

881 7590 02/10/2011

STITES & HARBISON PLLC
1199 NORTH FAIRFAX STREET
SUITE 900
ALEXANDRIA, VA 22314

EXAMINER	
OLSON, ERIC	

ART UNIT	PAPER NUMBER
1623	

NOTIFICATION DATE	DELIVERY MODE
02/10/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

iplaw@stites.com

Office Action Summary	Application No.	Applicant(s)	
	10/668,665	YVIN ET AL.	
	Examiner	Art Unit	
	ERIC S. OLSON	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 January 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-7,10 and 11* is/are pending in the application.

4a) Of the above claim(s) *11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-7 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

This office action is a response to applicant's communication submitted January 4, 2011 wherein claim 1 is amended. This application was filed September 23, 2003, and makes no priority claims.

Claims 1, 5-7, 10, and 11 are pending in this application.

Claim 11 is withdrawn from consideration as drawn to a non-elected invention.

Claims 1, 5-7, and 10 as amended are examined on the merits herein.

The following rejections of record in the previous office action are maintained:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 5-7, and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kong et al. (PCT International publication WO01/44263, Reference and English translation of record in previous action) in view of Shoji et al. (US patent 5498602, of record in previous action)

Kong et al. discloses oligosaccharides with immunostimulating and antitumor activity. (p. 6, first paragraph of the translation) The oligosaccharides fall within a general formula [I] that includes both branched (when m is 1-4) or unbranched (when m is 0) saccharides. (p. 6 last paragraph - p. 7 second paragraph of the translation) In a

preferred embodiment, the saccharides are all glucose and are linked by beta 1,3 linkages. (p. 7 paragraphs 5 and 6, p. 8 first paragraph, translation) Tetrasaccharides and pentasaccharides are preferred. (p. 8 third paragraph, translation) The oligosaccharides can be used in a method for treating cancer by injection or oral administration. (p. 22, third paragraph, translation) They work by inducing expression of LI-2 and TNF-alpha in the peripheral blood. (p. 22, last paragraph, translation) The saccharides are disclosed in pharmaceutical formulations comprising pharmaceutical solutions and tablets. (p. 45 last paragraph - p. 47 first paragraph, translation) Kong et al. does not explicitly disclose an unbranched saccharide having all the characteristics recited in the instant claims or a method of making said saccharide.

Shoji et al. discloses the isolation of laminaripentaose, which is the beta-glucan pentasaccharide of the claimed invention. (column 39 lines 17-30) This demonstrates that one skilled in the art is able to obtain this unbranched pentasaccharide.

It would have been obvious to one of ordinary skill in the art at the time of the invention to treat a subject in a method according to Kong et al. using an unbranched beta 1,3-glucan tetrasaccharide or pentasaccharide. One of ordinary skill in the art would have been motivated to use a 1,3-beta-glucan tetrasaccharides or pentasaccharide because all of these qualities (length, 1,3-beta bonds, glucose residues) are disclosed by Kong et al. as preferred embodiments of the invention. One of ordinary skill in the art would have been motivated to use an unbranched saccharide because Kong et al. discloses in formula [I] that the saccharides can be unbranched. One of ordinary skill in the art would reasonably have expected success because these

saccharides are included within the broad teaching of Kong et al. as having the disclosed antitumor activity.

Furthermore, regarding how one skilled in the art could obtain laminaripentaose oligosaccharide, Shoji et al. demonstrates that it is possible for one skilled in the art to obtain this unbranched oligosaccharide. Therefore one of ordinary skill in the art would have been able to make the pentasaccharide of the claimed invention in the same manner of Shoji et al.

Therefore the invention taken as a whole is *prima facie* obvious.

Claims 1, 5-7, and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kong et al. (PCT International publication WO01/44263, Reference and English translation of record in previous action) in view of Katsuraya et al. 1 (of record in previous action)

Kong et al. discloses oligosaccharides with immunostimulating and antitumor activity. (p. 6, first paragraph of the translation) The oligosaccharides fall within a general formula [I] that includes both branched (when m is 1-4) or unbranched (when m is 0) saccharides. (p. 6 last paragraph - p. 7 second paragraph of the translation) In a preferred embodiment, the saccharides are all glucose and are linked by beta 1,3 linkages. (p. 7 paragraphs 5 and 6, p. 8 first paragraph, translation) Tetrasaccharides and pentasaccharides are preferred. (p. 8 third paragraph, translation) The oligosaccharides can be used in a method for treating cancer by injection or oral administration. (p. 22, third paragraph, translation) They work by inducing expression of

LI-2 and TNF-alpha in the peripheral blood. (p. 22, last paragraph, translation) The saccharides are disclosed in pharmaceutical formulations comprising pharmaceutical solutions and tablets. (p. 45 last paragraph - p. 47 first paragraph, translation) Kong et al. does not explicitly disclose an unbranched saccharide having all the characteristics recited in the instant claims or a method of making said saccharide.

Katsuraya et al. 1 discloses a synthetic method involving the acetylation and glycosyl modification of oligosaccharides including laminaripentaose, one of the oligosaccharides included in the instant claims. (p. 53 scheme1) The laminaripentaose starting material was produced enzymatically using a bacterial enzyme. (p. 59 first paragraph) This demonstrates that one skilled in the art is able to obtain the claimed unbranched pentasaccharide.

It would have been obvious to one of ordinary skill in the art at the time of the invention to treat a subject in a method according to Kong et al. using an unbranched beta 1,3-glucan tetrasaccharide or pentasaccharide. One of ordinary skill in the art would have been motivated to use a 1,3-beta-glucan tetrasaccharides or pentasaccharide because all of these qualities (length, 1,3-beta bonds, glucose residues) are disclosed by Kong et al. as preferred embodiments of the invention. One of ordinary skill in the art would have been motivated to use an unbranched saccharide because Kong et al. discloses in formula [I] that the saccharides can be unbranched. One of ordinary skill in the art would reasonably have expected success because these saccharides are included within the broad teaching of Kong et al. as having the disclosed antitumor activity.

Furthermore, regarding how one skilled in the art could obtain laminaripentaose oligosaccharide, One of ordinary skill in the art would have been motivated to obtain this saccharide using the enzymatic method disclosed by Katsuraya et al. 1. Therefore one of ordinary skill in the art would have been able to make the pentasaccharide of the claimed invention in the same manner of Katsuraya et al.

Therefore the invention taken as a whole is *prima facie* obvious.

Claims 1, 5-7, and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kong et al. (PCT International publication WO01/44263, Reference and English translation of record in previous action) in view of Katsuraya et al. 2 (of record in previous action)

Kong et al. discloses oligosaccharides with immunostimulating and antitumor activity. (p. 6, first paragraph of the translation) The oligosaccharides fall within a general formula [I] that includes both branched (when m is 1-4) or unbranched (when m is 0) saccharides. (p. 6 last paragraph - p. 7 second paragraph of the translation) In a preferred embodiment, the saccharides are all glucose and are linked by beta 1,3 linkages. (p. 7 paragraphs 5 and 6, p. 8 first paragraph, translation) Tetrasaccharides and pentasaccharides are preferred. (p. 8 third paragraph, translation) The oligosaccharides can be used in a method for treating cancer by injection or oral administration. (p. 22, third paragraph, translation) They work by inducing expression of LI-2 and TNF-alpha in the peripheral blood. (p. 22, last paragraph, translation) The saccharides are disclosed in pharmaceutical formulations comprising pharmaceutical

solutions and tablets. (p. 45 last paragraph - p. 47 first paragraph, translation) Kong et al. does not explicitly disclose an unbranched saccharide having all the characteristics recited in the instant claims or a method of making said saccharide.

Katsuraya et al. 2 discloses that laminara-oligosaccharides having five or more 1,3-beta-glucosyl subunits can be made by chemical hydrolysis or acetolysis of curdlan. (p. 6696, left column scheme 1, left column third paragraph - right column first paragraph) This demonstrates that one skilled in the art is able to obtain the claimed unbranched pentasaccharide.

It would have been obvious to one of ordinary skill in the art at the time of the invention to treat a subject in a method according to Kong et al. using an unbranched beta 1,3-glucan tetrasaccharide or pentasaccharide. One of ordinary skill in the art would have been motivated to use a 1,3-beta-glucan tetrasaccharides or pentasaccharide because all of these qualities (length, 1,3-beta bonds, glucose residues) are disclosed by Kong et al. as preferred embodiments of the invention. One of ordinary skill in the art would have been motivated to use an unbranched saccharide because Kong et al. discloses in formula [I] that the saccharides can be unbranched. One of ordinary skill in the art would reasonably have expected success because these saccharides are included within the broad teaching of Kong et al. as having the disclosed antitumor activity.

Furthermore, regarding how one skilled in the art could obtain laminaripentaose oligosaccharide, One of ordinary skill in the art would have been motivated to obtain this saccharide using the enzymatic method disclosed by Katsuraya et al. 2. Therefore one

of ordinary skill in the art would have been able to make the pentasaccharide of the claimed invention in the same manner of Katsuraya et al.

Therefore the invention taken as a whole is *prima facie* obvious.

Claims 1, 5-7, and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kong et al. (PCT International publication WO01/44263, Reference and English translation of record in previous action) in view of Katsuraya et al. 3 (of record in previous action)

Kong et al. discloses oligosaccharides with immunostimulating and antitumor activity. (p. 6, first paragraph of the translation) The oligosaccharides fall within a general formula [I] that includes both branched (when m is 1-4) or unbranched (when m is 0) saccharides. (p. 6 last paragraph - p. 7 second paragraph of the translation) In a preferred embodiment, the saccharides are all glucose and are linked by beta 1,3 linkages. (p. 7 paragraphs 5 and 6, p. 8 first paragraph, translation) Tetrasaccharides and pentasaccharides are preferred. (p. 8 third paragraph, translation) The oligosaccharides can be used in a method for treating cancer by injection or oral administration. (p. 22, third paragraph, translation) They work by inducing expression of LI-2 and TNF-alpha in the peripheral blood. (p. 22, last paragraph, translation) The saccharides are disclosed in pharmaceutical formulations comprising pharmaceutical solutions and tablets. (p. 45 last paragraph - p. 47 first paragraph, translation) Kong et al. does not explicitly disclose an unbranched saccharide having all the characteristics recited in the instant claims or a method of making said saccharide.

Katsuraya et al. 3 discloses that laminaritetraose and laminaripentaose can be obtained by hydrolysis of curdlan. (abstract) This demonstrates that one skilled in the art is able to obtain the claimed unbranched pentasaccharide.

It would have been obvious to one of ordinary skill in the art at the time of the invention to treat a subject in a method according to Kong et al. using an unbranched beta 1,3-glucan tetrasaccharide or pentasaccharide. One of ordinary skill in the art would have been motivated to use a 1,3-beta-glucan tetrasaccharides or pentasaccharide because all of these qualities (length, 1,3-beta bonds, glucose residues) are disclosed by Kong et al. as preferred embodiments of the invention. One of ordinary skill in the art would have been motivated to use an unbranched saccharide because Kong et al. discloses in formula [I] that the saccharides can be unbranched. One of ordinary skill in the art would reasonably have expected success because these saccharides are included within the broad teaching of Kong et al. as having the disclosed antitumor activity.

Furthermore, regarding how one skilled in the art could obtain laminaritetraose or laminaripentaose oligosaccharides, One of ordinary skill in the art would have been motivated to obtain this saccharide using the enzymatic method disclosed by Katsuraya et al. 3. Therefore one of ordinary skill in the art would have been able to make the tetrasaccharide or pentasaccharide of the claimed invention in the same manner of Katsuraya et al.

Therefore the invention taken as a whole is *prima facie* obvious.

Response to Arguments

Applicant's arguments, submitted January 4, 2011, with respect to the above grounds of rejection, have been fully considered and not found to be persuasive to remove the rejections. With regard to all of the rejections, Applicant argues that the secondary reference is not enabling for the synthesis of laminara-oligosaccharides. In particular, Applicant argues that the oligosaccharides synthesized in the prior art contain a mixture of alpha and beta glycosidic linkages, and are therefore different from the oligosaccharides recited in the instant claims which contain only beta linkages. Based on this interpretation of the prior art, Applicant claims that the synthesis and isolation of oligosaccharides is unpredictable and that one skilled in the art would thus be unable to make the oligosaccharides used in the instant claims based on the cited prior art.

However, Applicant's interpretation of the prior art is incorrect. All of the cited prior art references refer to the oligosaccharides being produced as laminaritetraose or laminaripentaose. According to entries 26212-72-6 and 23743-55-7 of the Chemical Abstracts Registry (References included with PTO-892) these two oligosaccharides contain only 1-3 beta linkages. There are no alpha linkages in laminaritetraose or laminaripentaose and no compound containing alpha linkages between the glucosyl units is properly called by either of these names. This is verified by scheme 1 on p. 6696 of Katsuraya et al. 2, where the laminara-oligosaccharides are pictured as having only 1,3- beta linkages. While it is true that table 2 in this reference does include a beta/alpha ratio as one way in which acetylated laminara-oligosaccharides are characterized, this ratio refers not to the glycoside backbone 1,3 linkages, but rather to

the position of the 1-acetyloxy group at the reducing end of the peracetylated oligosaccharide. This view is supported by the discussion of stereochemistry at the reducing terminal on p. 6696 right column third paragraph of this reference. Furthermore, the references Katsuraya et al. 1 and 3 (of record in previous action) which are published by the same author, mention alpha stereochemistry only in the context of an alpha/beta ratio of peracetylated oligosaccharides and are reasonably interpreted in the same manner. Needless to say, in the non-acetylated oligosaccharide, this reducing end position exists as an -OH group in equilibrium between anomeric forms in the non-acetylated laminara-oligosaccharides, and therefore falls within the claimed structures.

Shoji et al. US5498602 similarly only refers to alpha stereochemistry in the context of peracetylated laminaripentaose. As laminaripentaose by definition contains only beta linkages, once more the only reasonable interpretation of the alpha stereochemistry is that it refers to the anomeric acetyl group rather than to an inter-saccharidic linkage. This is corroborated by the fact that the synthetic scheme in example 4 of this reference, in which the reference to alpha stereochemistry appears, is directed toward a method of making p-octylphenyl laminaripentaoside peracetate, which is described as p-octylphenyl-beta-D-glucopyranosyl-(1-3)-{beta-D-glucopyranosyl-(1-3)}$_3$ -beta-D-glucopyranoside peracetate. This product contains no alpha linkages. Since no intergylcosidic linkages are formed or broken during the synthesis, the starting material must therefore contain only beta interglycosidic linkages. As a result, one of ordinary skill in the art would conclude that it is the reducing end alpha-O-acetyl

glycosidic bond which is cleaved during the synthesis and then replaced with a beta-O-p-octylphenyl group.

Therefore it is clear that the terms "laminaripentaose" and "laminaritetraose" in the prior art references are referring to oligosaccharides containing only beta 1,3 linkages, which are the same oligosaccharides used in the claimed methods. As a result, one skilled in the art would clearly be able to obtain the claimed oligosaccharides, and would therefore be enabled to practice the claimed invention based solely on the prior art.

For these reasons the rejection is deemed proper and made **FINAL.**

Conclusion

No claims are allowed in this application. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ERIC S. OLSON whose telephone number is (571)272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Eric S Olson/
Primary Examiner, Art Unit 1623
2/2/2011